REMARKS

Claims 1-4, 8, 10, 12, 14, 20 and 28, were originally pending in this application. These claims are canceled herein and replaced with new claims 30 to 51 which further clarify and define the Applicants' invention; claims 30 to 51 are now pending in this case. New claims are submitted to more precisely describe what the Applicants believe to be the subject matter of their invention, and support for the new claims can be found throughout the application as filed. Specifically, support for claims 30 to 51 can be found throughout the specification. In particular, support for claim 30 can be found for SEQ ID No 2 in Figure 22; page 8, lines 25-35; page 9, lines 17-21; page 11, line 25 to page 12, line 13; and the leader sequence on page 29, lines 8-9 and lines 21-22. Support for claim 31 can be found on page 8, lines 25-35. Support for claim 32 can be found on page 10, lines 14-17. Support for claim 33 can be found on page 10, lines 7-13. Support for claim 34 can be found on page 50, lines 6 - 8. Support for claim 35 can be found on page 29, lines 8-9, page 29, lines 21-22, page 32, lines 34-35, page 50, lines 6-10. Support for claim 36 can be found on page 4, lines 10- 12; and page 12, lines 23-38. Support for claim 37 can be found on page 4, lines 12-5; and page 13, lines 11-16. Support for claim 48 can be found on page 5, lines 1-7. Support for claim 38 can be found on page 4, lines 16-17 and lines 19-25; page 12, lines 22-38; and page 13, lines 17-20. Support for claim 39 can be found on page 4, lines 10-15; and page 13, lines 17-20. Support for claim 40 can be found on page 4, lines 19-25. Support for claim 41 can be

found on page 5, lines 31-34. Support for claim 42 can be found on page 13, line 28 - page 14, line 6. Support for claim 43 can be found on page 5, lines 1-7. Support for claim 44 can be found on page 10, lines 7-23. Support for claim 45 can be found on page 11, lines 3-6. Support for claim 46 can be found on page 3, line 35 to page 4, line 6. Support for claim 47 can be found on page 4, lines 12-15; and page 13, lines 11-16. Support for claim 48 can be found on page 5, lines 1-7. Support for claim 49 can be found on page 3, lines 19-21; and page 18, lines 16-22. Support for claim 50 can be found on page 18, lines 16-22. Support for claim 51 can be found on page 3, lines 19-21; page 6, lines 19-23; and page 18, lines 16-22. Accordingly, the Applicants believe that no new matter has been introduced into this application as a result of the present amendment.

THE REJECTIONS

Turning to the Office Action, claims 1 - 4, 8, and10 stand rejected under 35 U.S.C. §102(b) as being anticipated by Murphy et al., J. Clin. Microbiol. Sept 1993, vol. 31, no. 9, 2303-2308 ("Murphy"); claims 1-4, 8, 10 and 12, 14, 20 and 28 stand rejected under 35 U.S.C. §103 as obvious over Murphy in view of Loosmore et al., IDS:WO 95/13370, May 18, 1995 ("Loosmore"); claims 4, 8 and 10 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention; and claims 1-2, 12 and 20 stand

rejected under 35 U.S.C. §112, first paragraph for lack of enablement. Applicants respectfully traverse these rejections as originally asserted and as they might be applied to new claims 30-51.

REJECTION UNDER 35 U.S.C. §102(b)

Claims 1-4, 8, and10 stand rejected under 35 U.S.C. §102(b) as being anticipated by Murphy. The Examiner contends that said claims read over Murphy because these claims did not identify any SEQ ID NO. Moreover the Examiner objected to claiming a transferrin binding protein in the absence of characterization of protein. Finally, the Examiner contends that although SEQ ID NO:1 or sequence 80% homologous thereto in claim 4 is not disclosed, claim 4 still reads over Murphy because the chromosomal DNA disclosed by Murphy inherently encodes the claimed sequence and thus meets the structural requirement of claim 4.

In order to qualify as prior art under section 102(b) the reference must teach each and every element of the claimed invention. While Murphy's teachings incorporates some of the same elements as the applicants, the presently claimed invention is significantly different from Murphy's disclosure in a number of ways.

Applicants respectfully submit that new claim 30 does not read on the prior art. Murphy disclosed isolation and purification of total cell DNA from *P. hemolytica* and hybridization with a probe which is a naturally occurring nucleic acid molecule inherently

containing complementary sequences that inherently encodes a transferrin binding protein and is capable of hybridizing under stringent hybridization conditions. It is well known to one skilled in the art that the conditions used by Murphy, (lines 4-17, page 2304) cause cell breakage and damage to the chromosome, such that it can not be said with certainty that Murphy isolated one molecule comprising the gene of the present invention. Extracting full length/intact chromosomal DNA requires special procedures which were not used in this case. Applicants submit that two publications describe the types of conditions which must be used to extract full length/intact chromosomal DNA from *E. coli* and *Salmonella*, which applies to most, if not all Gram-negative bacteria, including *P. haemolytica* A1 (Pettijohn, D., Cell. & Mol. Biol. 2nd Ed.,. p158-199, 1996; QIAGEN Genomic DNA Handbook, p 8-9, 9/1997). Applicants draw the Examiner's attention to page 161 of the Pettijohn publication, wherein the DNA shown in the electron micrographs contains numerous nicks and single-strand breaks that were generated in order to unfold the DNA molecule. Since the DNA is highly folded and compact and requires unfolding, Applicant asserts that it is nearly impossible to isolate the complete DNA without creating breakage; the recovered DNA is always in smaller sections.

Moreover, it is also important to note that 73% of the isolates carried one plasmid and 13.5% of the isolates carried two plasmids; these plasmids were included with the DNA isolated. Thus, even if Murphy used special procedures to isolate a full length/intact

chromosome, in 86.5% of the cases, Murphy did not isolate "an isolated polynucleotide comprising . . .a polynucleotide encoding a TbpA polypeptide of *P. haemolytica* . . ." Rather, Murphy isolated "an isolated polynucleotide" from specific serotypes of *P. haemolytica* that do not contain any plasmids.

Thus, applicants submit that the wording of the claims does not read on Murphy, because the generalized wording of the claimed statement (ie. each and every time, an isolated polynucleotide can be obtained comprising a polynucleotide sequence coding for TbpA) can not be applied in general to Murphy. In fact, even if the special procedures were used to extract full length/intact chromosomal DNA, this statement would be incorrect 86.5% of the time due to the presence of plasmid DNA.

Applicants further respectfully submit that Murphy disclosed isolation of total cellular DNA from *P. haemolytica* but did not disclose purification of the molecule encoding the transferrin binding protein. The preparation of genomic DNA that Murphy describes contains thousands of genes encoded by this bacterium and there is no enrichment or purification of the gene encoding the transferrin binding protein relative to any of the other genes. Although the preparation of genomic DNA contains the nucleic acid region that encodes the transferrin binding protein, so does in fact the intact organism.

Thus, Murphy does not teach an isolated polynucleotide comprising a polynucleotide having at least 80% identity to a member selected from the group consisting of: (a) a

polynucleotide encoding a TbpA polypeptide of *P. haemolytica* comprising an amino acid sequence as set forth in SEQ ID NO:2; (b) a polynucleotide encoding a TbpA polypeptide of *P. haemolytica* comprising amino acid 1 to amino acid 930 as set forth in SEQ ID NO:2; (c) a polynucleotide encoding a TbpA polypeptide of *P. haemolytica* comprising amino acid 29 to amino acid 930 as set forth in SEQ ID NO:2; and (d) a polynucleotide which is complementary to the polynucleotide of (a), (b) or (c). Murphy does not teach any amino acid sequences for a transferrin binding protein, nor does Murphy teach an isolated polynucleotide coding for such amino acid sequence, with or without its putative leader sequence. Although the chromosomal DNA of the organism from which Murphy isolated his samples inherently encodes the claimed sequence, the cell-free materials of Murphy do not provide the claimed invention. Furthermore, the materials prepared by Murphy do not include isolated RNA (claim 32) or vectors comprising TbpA sequences (claim 36).

Applicants respectfully submits that the §102(b) rejections no longer apply for these reasons and in light of the present amendments, and request withdrawal of the §102(b) rejections.

REJECTION UNDER 35 U.S.C. §103

Claims 1 - 4, 8, 10 and 12, 14, 20 and 28 stand rejected under 35 U.S.C. §103 as obvious over Murphy in view of Loosmore. The Examiner contends that it would have been obvious to use

the methods taught by Loosmore, combined with Murphy to isolate the claimed gene from *P. haemolytica*. Applicants respectfully traverse this rejection.

One of the requirements of establishing a *prima facie* case of obviousness under 35 U.S.C. §103 is the requirement that the prior art reference or combination of references must teach or suggest all the limitations of the claims. See *In re Wilson*, 424 F.2d 1382,1385, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970) ("All words in a claim must be considered in judging the patentability of that claim against the prior art."). And the teachings or suggestions, as well as the expectation of success, must come from the prior art, not applicant's disclosure. See *In re Vaeck,* 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991).

Applicants respectfully submit that the claimed invention not obvious from the combined teachings of Murphy with Loosmore. Applicants respectfully submit that the combination Murphy and Loosmore actually teach away from the present invention.

In addition to the arguments provided above, regarding the inclusion of plasmid DNA in 86.5% of the isolates, Murphy teaches that there are many genetic differences between different serotypes of *P. haemolytica*. For Example, Murphy states, "The data reveal the presence of genetic differences among isolates of *P. haemolytica* A1 associated with shipping fever pneumonia within a closed feedlot, and suggest that a combination of REA, ribotyping, plasmid analysis, and antibiotic susceptibility determination will be useful in analyzing the molecular epidemology of this disease (Abstract, p. 2303) and "Here, our analyses of plasmid

content and antimicrobial susceptibility suggest further differences between *P. haemolytica* A1 isolates of a given RT or REA type (line 22 - 25, page 2307)." Thus, Applicants submit that Murphy teaches that there are numerous differences between serotypes of *P. haemolytica* that become even more apparent on the genetic level.

Loosmore teaches "The nucleic acid molecules provided herein are useful for the specific detection of strains of *Haemophilus*, and for diagnosis of infection by *Haemophilus*" (page 4, line 32 - 35), and on page 5, line 31 to page 6, line 3, ". . . there is provided a purified and isolated nucleic acid molecule encoding a transferrin receptor protein of a strain of *Haemophilus*, more particularly, a strain of *H. influenzae,* specifically a strain of *H. influenzae* type b, such as *H. influenzae* type b strain DL63, Eagan or MinnA, or a non-typable strain of *H. influenzae*, such as *H. influenzAe* strain PAK 12085, SB33, SB12, SB29, SB30 or SB32,. . ." Thus, Loosmore's invention provides a nucleic acid molecule pertaining to a specific bacterial group, for which, as stated previously, Applicants found that there is greater than 85% amino acid identity among the TbpA proteins from *P. haemolytica*, whereas there is only 40% homology between the TbpA sequence of *Haemophilus influenza* and *P. haemolytica*.

Moreover, the Examiner contends that 40% sequence homology is sufficient to isolate the gene as claimed under stringent hybridization conditions. One skilled in the art, appreciates that these conditions would not be reliable for methods of cloning, would result in numerous artifacts, and would therefore teach away from the present invention. It is taught

in Maniatis et al. (Molecular Cloning: A Laboratory Manual, Cold Spring Harbor, 1st edition, p. 387-389, 1982) that "if the homology between the probe and the DNA bound to the filter is inexact, the washing should be carried out under less stringent conditions. . ." Maniatis et al. further teaches that the Tm decreases by 1 degree centigrade with every 1% in the number of mismatched bases, thus, for a molecule with 40% homology, this would result in a decrease in in Tm of 60 degrees; this is clearly not a situation wherein one skilled in the art would desire to use "stringent" conditions. Moreover, a similar effect would be seen with ionic strength of the wash solution. These conditions would not lead one to the gene as claimed in claim 30 *et seq*.

Applicants submit that Murphy and Loosmore, whether alone or together, neither teach nor suggest the invention as presently claimed. Therefore, it is respectfully requested that the objection under 35 U.S.C. §103(a) be withdrawn.

REJECTION UNDER 35 U.S.C. §112, SECOND PARAGRAPH

Claims 4, 8 and 10 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants respectfully submit that the §112, second paragraph rejections no longer apply in light of the present amendments.

Moreover, Applicants submit that a variety of known algorithms are disclosed publically and a variety of commercially available software for conducting search means are and can be used in computer based means of comparison. Examples of such software includes, but is not limited to MacPattern (EMBL), BLASTIN and BLASTX (NCBIA). A skilled artisan can readily recognize that any one of the available algorhithms or implementing software packages can be used for conducting homology searches. There are also a variety of comparing means that can be used to compare a target sequence or target motif with a data storage means to identify sequence fragments. Implementing software which implements the BLAST and BLAZE algorithms (eg. as described in Altschul et al., 1990, J. Mol. Biol. 215:403-410) can be used.

In view of the present amendments, Applicants respectfully request that the rejection under 35 U.S.C. §112, second paragraph, be withdrawn.

REJECTION UNDER 35 U.S.C. §112, FIRST PARAGRAPH

Claims 1 - 2, 12 and 20 remain rejected under 35 U.S.C. 112, first paragraph, for lack of enablement. In particular, the Examiner states that the specification lacks guidance, examples and there is a lack of predictability associated with regard to expressing proteins, inducing an immunological response and using the myriad of fragments encompassed in the scope of the claims such that one skilled in the art would be forced into undue

experimentation in order to practice broadly the claimed invention. Applicants respectfully submit that the §112, first paragraph, rejections no longer apply in light of the present amendments which more precisely define the subject matter invention, and therefore the rejection should be withdrawn.

Applicants respectfully request reconsideration of the subject Continued Prosecution Application in view of the above amendments and remarks.

Respectfully submitted,
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